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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,485	03/08/2001	Erin B. Dickerson	WARF-0003	4744

26259 7590 08/11/2003

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MARLTON, NJ 08053

EXAMINER

SEHARASEYON, JEGATHEESAN

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 08/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application N .</b>		<b>Applicant(s)</b>	
	09/801,485		DICKERSON ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Jegatheesan Seharaseyon		1647	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on 24 April 2003.

2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) 1-9 is/are pending in the application.

4a) Of the above claim(s) 7-9 is/are withdrawn from consideration.

5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.

6) ☒ Claim(s) 1-6 is/are rejected.

7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.

8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All   b) ☐ Some \* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>5</u> .	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6) <input type="checkbox"/> Other:
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### **DETAILED ACTION**

1. This office action is response to Applicant's election of group I, claims 1-3 drawn to a fusion protein comprising a mammalian interleukin-12 operably linked to a RGD-containing peptide.

Election was made with traverse in Paper No. 11 (4/24/03). The traversal is on the ground(s) that the search of all claims would not impose a serious burden on the Office because the groups are NOT distinct and unobvious. Applicants also assert that the examiner has indicated that all the claims are related to targeting interleukin-12 to malignant endothelium. There is no evidence for this in the previous Office Action (Paper No: 10). Groups I and II are directed to the fusion protein and the nucleotides encoding the same. Groups III, IV and V are directed to methods of using the fusion protein. Therefore, the searches for each of the groups are not coextensive and would be a burden on the office to search. However, the office will join Groups I and II because the nucleotides of Group II are needed for the synthesis of the fusion protein of Group I. Therefore, the restriction requirement is deemed proper and made FINAL.

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

### ***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3a. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (U.S. Patent No: 5,994,104) in view of Ruoslahti et al. (U.S. Patent No: 5,994,104).

The instant invention is directed to an interleukin-12 fusion protein comprising a RGD-containing peptide.

Anderson et al. teaches interleukin-12 fusion protein and nucleic acid constructs encoding them, and to the use of such fusion proteins in cancer therapy (see abstract). The invention provides: a nucleic acid construct comprising a coding region encoding an interleukin-12 (IL-12) fusion protein, said fusion protein comprising: (a) an IL-12 p35 subunit; (b) an IL-12 p40 subunit; and joining said subunits, a linker peptide; vectors and cell (column 2, line 61- column 3 line 9). In addition, it is stated that rIL-12 has demonstrated potent anti-tumor effects and has the best therapeutic effects when delivered at the site of tumor (column 1 lines: 53-58). However, Anderson et al.

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reference does not describe interleukin-12 operably linked to a RGD-containing peptide that can be targeted to tumor cells.

Ruoslahti et al. discloses the RGD sequence (SEQ ID NO: 1) also known as RGD-4C (column 33 lines: 14-30). The RGD peptide binds to human  $\alpha_V$  - integrins, which are selectively expressed in the in tumor blood vessels of patients (column 32 lines: 54-57). It also teaches the targeting of RGD conjugated doxorubicin to tumors (column 34 lines: 63-67). Ruoslahti et al. also disclose the pronounced destruction (3X greater) of the vasculature in the tumor treated with conjugate as compared to mice treated with free doxorubicin (column 35 lines: 1-8). Furthermore, it is stated that the administration to a tumor bearing mouse of a conjugate comprising a chemotherapeutic agent linked to a tumor homing molecule is more efficacious than administration of the agent, alone, in treating tumor (column 35 lines: 8-12). Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to operably link interleukin-12 disclosed in Anderson et al. to a RGD-containing peptide protein described in Ruoslahti et al. to produce a fusion protein conjugate capable binding to  $\alpha_V$  - integrins receptor on the surface of tumor blood vessels sufficient to destroy the blood vessels and cause tumor necrosis, because <sup>Anderson</sup> ~~Ruoslahti~~ et al. teaches that a <sup>IL-12 has potent anti-tumor effects</sup> chemotherapeutic agent linked to a tumor homing molecule is more efficacious than administration of the agent, alone, in treating a tumor. Therefore, the instant invention is <sup>unpatented</sup> Anderson et al. (U.S. Patent No: 5,994,104) in view of Ruoslahti et al. (U.S. Patent No: 5,994,104).

4. No claims are allowable over prior art.

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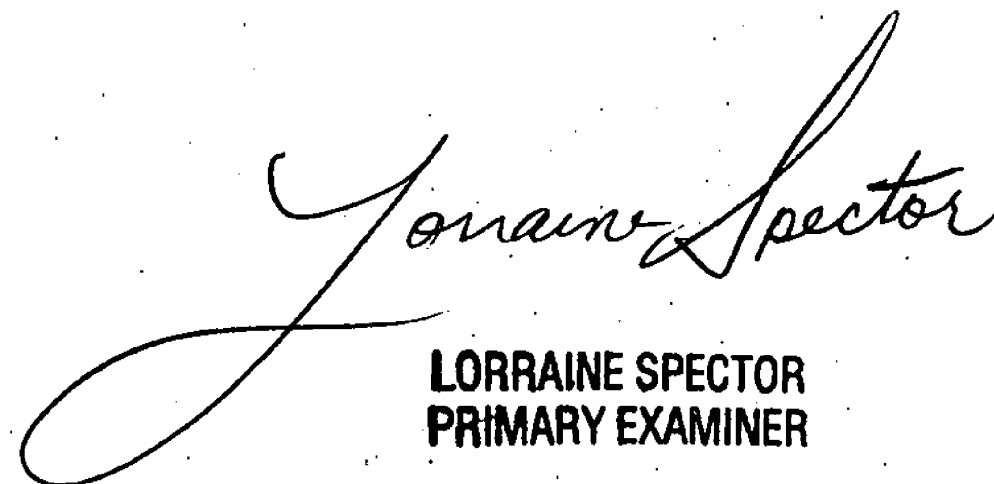
### **Contact Information**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and 703-308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JS  
August 5, 2003

  
**LORRAINE SPECTOR  
PRIMARY EXAMINER**